November 22, 2002

Kevin N. Baer, Ph.D.
Department of Toxicology
The University of Louisiana at Monroe
700 University Avenue
Monroe, LA 71209

(For Deltech Corporation)

Dear Dr. Baer:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Vinyl Toluene posted on the ChemRTK HPV Challenge Program Web site on July 24, 2002. I commend Deltech Corporation for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Deltech Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Vinyl Toluene

SUMMARY OF EPA COMMENTS

The sponsor, Deltech Corporation, submitted the test plan and robust summaries for vinyl toluene (CAS No. 25013-15-4) dated June 28, 2002. EPA posted the submission on the Chemical RTK HPV Challenge Website on July 24, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Except for biodegradation, EPA agrees that available data are adequate for the purposes of the HPV Challenge program for these endpoints. The submitter needs to perform a biodegradation study of vinyl toluene in a closed system to adequately address this endpoint.

2. Health Effects. The submitter discussed data on vinyl toluene in the test plan. However, robust summaries were not submitted for acute, reproductive, developmental, and genetic toxicity studies on this chemical. EPA will reserve judgement on adequacy of these endpoints pending submission and evaluation of these data.

3. Ecological Effects. Data are adequate for all endpoints for the purposes of the U.S. HPV Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE VINYL TOLUENE CHALLENGE SUBMISSION

Test Plan

The test plan was very difficult to follow for the following reasons: (1) The first part of the submission (pages 1 - 9) appears to be the test plan for this chemical but the information on the analog chemicals appears to be more the primary focus of the discussion than that of the subject chemical. In addition, this part of the test plan did not include references for many of the studies mentioned. (2) Pages 10 - 17 are a selection of brief summaries for vinyl toluene in varying degrees of detail. (3) Although robust summaries were included for para-ethylstyrene, the test plan did not describe the use of para-ethylstyrene as an analog chemical for vinyl toluene. (4) The submitter's comparison of the data for vinyl toluene and the analogs is unclear. For example, the submitter stated that comparisons were made for chronic toxicity; however, no information was presented in the test plan on the chronic toxicity of any of the analogs. It would have been helpful had the submitter provided a tabular comparison of the available data for vinyl toluene and all analogs. The submitter needs to address these areas to permit an adequate evaluation of the test plan, particularly for health effects.

Commercial vinyl toluene is a mixture of the meta and para isomers of methyl styrene in ~60/40% ratio. The test plan discussed data on this mixture for most health effects endpoints and compared them with styrene and para-methyl styrene analogs. However, robust summaries were not submitted on vinyl toluene for acute, reproductive, developmental and genetic toxicity studies. The submitter stated that toxicological properties and main metabolites of meta-, orhto-,and para-methylstyrene are similar to those of styrene, so that data available for para-methylstyrene and/or styrene would substitute for any vinyl toluene data gaps. EPA considers this approach appropriate; however, EPA recommends that the submitter provide robust summaries for available studies on vinyl toluene because there are no data on meta-methylstyrene and its proportion in vinyl toluene is significantly larger than the para isomer (60:40). Although no reproductive toxicity studies were available on vinyl toluene, documentation of evaluation of reproductive organs from the repeated-dose toxicity studies would be sufficient to address this endpoint for the purposes of the HPV Challenge Program, provided an adequate robust summary for developmental toxicity study is also submitted.

Chemistry (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

EPA agrees with the submitter that adequate data are available and no additional testing is necessary for

these endpoints for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Stability in Water. The submitter needs to state the rationale for not testing the hydrolysis of vinyl toluene. Vinyl toluene does not have a functional group that is susceptible to hydrolysis and so hydrolysis is not expected to occur in the environment. The submitter needs to add such language to the test plan.

Biodegradation. Data were provided in the submission for two surrogates of vinyl toluene (i.e., styrene, *p*-methylstyrene), the latter of which is an HPV Challenge chemical and makes up 40% of the commercial mixture. The studies for both surrogates are inadequate to address this endpoint. The styrene study did not follow standard guidelines. In addition, EPA agrees with the submitter that there was a high rate of loss from the reaction vessel due to the volatility of *p*-methylstyrene; the submitter needs to provide measured data obtained in a closed system. The same comment was made with regard to *p*-methylstyrene, also an HPV Challenge chemical. A closed system study should minimize the effects of volatilization and provide a true measure of the biodegradation of this chemical.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

It appears that data on vinyl toluene may be available to address all endpoints (with the possible exception of the reproductive toxicity endpoint). However, the submitter needs to provide full robust summaries for acute, genetic, reproductive, and developmental toxicity studies. EPA reserves judgement on data adequacy pending submission and evaluation of these study summaries.

Data for para-methyl styrene, which can be used as supporting data for the vinyl toluene toxicity studies, are adequate (refer to EPA's November 28, 2001 comments on the HPV Challenge submission for this chemical). Therefore, these data can be used to satisfy data gaps.

For styrene, no adequate fertility studies were identified, although a developmental toxicity study was considered to be well-conducted. Therefore, although some data for styrene may be used as support for vinyl toluene, these data should also be used with caution and should be further evaluated if the vinyl toluene data prove inadequate.

Acute toxicity. A brief mention of NTP acute toxicity data on vinyl toluene was given in the first part of the "Summaries" file, but the submitter stated that these data were not reviewed. No robust summaries of the vinyl toluene studies were submitted.

Although some deficiencies were noted in the robust summaries for para-methyl styrene and para-ethyltoluene, they are considered adequate for the purposes of the HPV Challenge program. One study notes that acute toxicity of para-methyl styrene was compared with 'cosden' vinyl toluene. The submitter needs to identify 'cosden' vinyl toluene and present the comparison of results with para-methyl styrene.

Genotoxicity (gene mutations). Several studies on vinyl toluene were discussed in the second portion of the test plan (Section 5.5 of the "Summaries" file). These data could not be evaluated because no robust summaries were submitted.

Genotoxicity (chromosomal aberrations). The test plan discusses several studies on vinyl toluene, but no robust summaries were presented.

Reproductive toxicity. No data were submitted for vinyl toluene. For this endpoint, the submitter needs to discuss any findings on reproductive organs from the repeated-dose studies on vinyl toluene, if available. In addition, the submitter should discuss effects seen at doses higher than the NOAEL for the 2-generation reproduction study on para-methyl styrene. The 3-generation reproductive toxicity study on styrene cannot be used alone to address this endpoint because 250 ppm (35 mg/kg/day), the highest dose tested, was also a NOEL.

Developmental toxicity. Three studies on vinyl toluene were mentioned in the test plan and short descriptions were given in the first part of the "Summaries" file; however, these data could not be evaluated because no robust summaries or references were provided for any of the studies. One of these studies indicates that vinyl toluene is a developmental toxicant in guinea pigs.

Ecological Effects (fish, invertebrate and algal toxicity).

The data submitted (for the surrogate compound p-methylstyrene) are adequate for these endpoints for the purposes of the HPV Challenge Program.

Specific Comments on Robust Summaries

Environmental Fate and Pathways

Water Stability. An explanation for not testing vinyl toluene for hydrolysis should be provided in the robust summary.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

As stated above, the submitter needs to provide robust summaries for acute toxicity, genetic toxicity, and developmental toxicity studies on vinyl toluene studies.

Repeated-dose toxicity. The submitter needs to provide statistical significance for some effects (e.g., body weight changes) in the 13-week inhalation rat and mouse data on vinyl toluene, if this study is chosen as the critical study for this endpoint.
Reproductive toxicity. If available, the submitter needs to prepare robust summaries of histopathological findings on reproductive organs from the 13-week vinyl toluene repeated-dose toxicity study.

Ecological Effects (fish, invertebrate and algal toxicity).

Invertebrate. p-Methylstyrene, test article ID# MCTR-197-79: missing data element is dissolved oxygen content.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.